10/501 536
7-16-04

PRV

PATENT- OCH REGISTRERINGSVERKET
Patentavdelningen

PCT/SE 02 / 0 2 3 6 5

REC'D 15 JAN 2003
WIPO PCT

Intyg
Certificate

PATENT- OCH REGISTRERINGSVERKET

Härmed intygas att bifogade kopior överensstämmer med de handlingar som ursprungligen ingivits till Patent- och registreringsverket i nedannämnda ansökan.

This is to certify that the annexed is a true copy of the documents as originally filed with the Patent- and Registration Office in connection with the following patent application.

(71) Sökande Applicant (s) — *Radi Medical Systems AB, Uppsala SE*

(21) Patentansökningsnummer Patent application number — *0200293-9*

(86) Ingivningsdatum Date of filing — *2002-01-31*

BEST AVAILABLE COPY

Stockholm, 2003-01-08

För Patent- och registreringsverket
For the Patent- and Registration Office

Lina Oljeqvist

Lina Oljeqvist

Avgift
Fee

PRIORITY DOCUMENT
SUBMITTED OR TRANSMITTED IN COMPLIANCE WITH RULE 17.1(a) OR (b)

PATENT- OCH REGISTRERINGSVERKET
SWEDEN

Postadress/Adress
Box 5055
S-102 42 STOCKHOLM

Telefon/Phone
+46 8 782 25 00
Vx 08-782 25 00

Telex
17978
PATOREG S

Telefax
+46 8 666 02 86
08-666 02 86

Field of the invention

The present invention relates generally to the field of metal stents for insertion into vessels in the body, and particularly to dissolvable metal stents being made of a metal that dissolves by corrosion inside the body vessel and to disintegrating metal stents being made of two metals with different electrochemical potentials, thereby forming a galvanic element in which an electrochemical reaction occurs that consumes the metal having the lower electrochemical potential.

Background of the invention

A number of different stents have been proposed for the stenting of a blood vessel that has been occluded. A widely used type of stent consists of an expandable metal mesh. This type of stent may be further divided into self-expanding stents and non-self-expanding stents. The self-expanding stents can be made of a mesh material that changes to a larger-size configuration upon heating to body temperature. Examples of stents of this type may be found in US 6,071,308. Other self-expanding mesh stents are made of a resilient material, which can be flexed down into a small diameter tube and held in place in this configuration until it is released, at which time the mesh expands to the larger configuration. The non-self-expanding stents are often expanded by use of an inflatable balloon, which is placed inside the mesh being in the small diameter configuration and which is then inflated, thereby expanding the mesh to the large diameter configuration. The balloon itself is then deflated for removal, while the metal mesh is left in the expanded configuration. For examples of non-self-expanding stents, see US patent no. 5,799,384 and the international application WO 0189417.

Some of this expandable metal mesh stents are combined with an expandable polymer layer, which may be positioned on the inside of the expandable mesh, on the outside of the expandable mesh, within the interstices of the expandable mesh, or any combination of inside, outside and within the interstices of the expandable mesh stent. A stent of this type is, for example, shown in US 5,968,070, wherein the polymer layer may consist of expanded polytetrafluoroethylene (PTFE). As disclosed in, for example, US 5,160,341, it is also possible to use a polymer layer made of a resorbable polymer, such as polylactic acid homopolymers, polyglycolic acid homopolymers, or copolymers of polylactic acid and polyglycolic acid.

One advantage with expandable metal mesh stents is that their small diameter in the pre-expanded state allows easy insertion into narrow vessels. However, after the expansion, the metal mesh stents are difficult to remove since tissue in-growth occurs over time, and, in praxis, the stents are normally left inside the blood vessel. The main complication associated with the stenting of a stenosis in a blood vessel is the risk of having a restenosis, in which case a new stenosis develops at the same position as the first one, i.e. a new stenosis is growing inside the inserted stent. Several types of stents have been suggested to handle this severe problem, including drug-delivering stents and radioactive stents. Examples of drug-delivering stents may be found in US 6,206,195, while examples of stents for radiotherapy may be found in US 6,192,271. Nevertheless, there is still a substantial risk of having a restenosis following the stenting of a coronary artery. In this case, a second stent is normally

inserted and expanded inside the first one, which obviously reduces the diameter of the second stent in its expanded configuration as well as the inner diameter of the re-stented blood vessel.

Further, when a stent is placed permanently inside a coronary artery, the continuous stress from the beating of the heart may cause the wall and edges of the stent to damage the vessel wall. This damage can lead to arterial rupture or aneurysm formation. Also, a stent adapted to be permanently implanted within a blood vessel is continuously exposed to the flow of blood inside the vessel, which may lead to thrombus formation within the blood vessel. Stents made of absorbable materials (see e.g. US 5,306,286) have been proposed in order to overcome these problems. A disadvantage with such stents is that they are difficult to expand, i.e. they are of the self-expandable type. They have also a limited capability to withstand the compressive pressure exerted by the blood vessel in their expanded configuration.

It would therefore be desirable to provide a stent that combines the expandability and structural integrity of the metal mesh stents with the advantages of the absorbable stents. Such a stent would allow easy insertion into the blood vessel and yet being expandable enough to expand the blood vessel to the desired volume. The stent should also avoid the complications associated with permanently implanted stents by becoming dissolved or disintegrated. A stent having these characteristics would allow stenting of a restenosis, with the final inner diameter of the re-stented blood vessel being the same as after the first stenting operation.

Summary of the invention

The object of the present invention is to provide a metal stent, which dissolves or disintegrates inside a blood vessel after a predefined time. In a first embodiment, the stent comprises a metal mesh made of a metal that dissolves by corrosion in the environment prevailing within the blood vessel. In a second embodiment, the metal mesh is made of at least two metals having different electrochemical potentials, thereby forming an active galvanic element. In the galvanic element, an electrochemical reaction occurs, which consumes the metal having the lower electrochemical potential. If the joints of the metal mesh are made of the metal having the lower electrochemical potential, these joints will dissolve, which leaves the rest of the mesh in a disintegrated configuration.

This object is achieved with a stent according to claim 1. Preferred embodiments of the dissolvable or disintegrating stent according to the invention are defined in the dependent claims.

Brief description of the drawings

Fig. 1 shows a first embodiment of an expandable metal mesh stent according to the invention.

Fig. 2 shows a second embodiment of an expandable metal mesh stent according to the invention.

Fig. 3 shows the stent of Fig. 2 in a disintegrated state.

Fig. 4 shows a third embodiment of an expandable metal mesh stent according to the invention.

Fig. 5 shows a cross-section of the stent of Fig. 4.

Detailed description of the drawings

Fig. 1 illustrates a first embodiment of an inventive stent. In Fig. 1, a stent 1 comprises a mesh 2 made of metal that corrodes in the environment prevailing inside a vessel. By choosing a suitable metal, it is possible to control the time elapsed until the stent is dissolved by corrosion inside the vessel. Obviously, this time depends on the physiological and chemical characteristics of both the vessel itself and the fluid flowing inside the vessel as well as for how long time it is necessary to support the stented vessel. A perhaps natural choice of metal would in this case be iron, or possibly an alloy of iron and a small amount of chromium or nickel in order to make the stent more resistant to corrosion, i.e. prolong the time before the stent is dissolved inside the vessel. In practise, the choice of metal or alloy may be tailored to the actual application.

A second embodiment of an inventive stent is illustrated in Fig. 2. Here, a stent 3 comprises a metal mesh 4, which comprises two component parts, joints 5 and straight portions 6. If the joints 5 are made of metal having a lower electrochemical potential than the metal of the straight portions 6, an active galvanic element is created, with the fluid inside the vessel acting as an electrolyte. This galvanic element drives an electrochemical process, in which the metal having the lower electrochemical potential is consumed, which, in this case, means that the joints 5 of the mesh 4 are dissolved, thereby leaving the mesh 4 in a disintegrated configuration. This disintegrated configuration is shown in Fig. 3. As is well known, the kinetics of corrosion reactions may in actual practise differ from that predicted by electrochemical potentials in standard electrochemical series. When deciding metal combinations, one must therefore also take into account the characteristics of the vessel in question.

In the second embodiment described above, the joints 5 could, for example, consist of zinc while the straight portions 6 consist of iron. With this material combination, the whole stent 3 would eventually be dissolved since the straight portions 6 would dissolve by corrosion when the joints 5 have been consumed in the electrochemical process of the galvanic element. Another possibility is to make the mesh 4 of a first metal, such as iron, and then provide a layer of a second metal, such as gold, having a higher electrochemical potential at the joints 5. This configuration would create an electrochemical process in which the first metal (e.g. iron) is consumed beneath the layer of the second metal (e.g. gold). This combination would yield the same disintegrated configuration as shown in Fig. 3, the only difference being the small remainders of the second metal at the joints 5. In practise, the remaining amounts of the second metal can be made negligible small. As before, the specific materials and

material combinations can be tailored to the desired time before disintegration of the stent. It is, of course, also possible to provide the two metals at other positions than the joints and straight portions of the mesh, which would leave the disintegrated stent in some other configuration than the one shown in Fig. 3. Further, the metal mesh could be made of more than two metals with different electrochemical potentials. If, for example three metals were used, two different galvanic elements would be created, which provides additional possibilities to adapt the disintegrations rates of the metal meshes as well as the disintegrated configurations to the specific application conditions.

A method of manufacturing stents is by direct laser cutting from a single metal tube. For the inventive purposes, this method could be applied on a tube made of two metals. Fig 4 illustrates a stent 7, which has been laser-cut to a desired mesh structure 8. As is shown in cross-section in Fig. 5, the stent 7 is made from a metal tube comprising a first layer 9 of first metal, such as stainless steel, and a second layer 10 of a second metal, such as platinum, the second metal having a higher electrochemical potential than the first metal. For clarity of illustration, the two layers have been enlarged in Fig. 5. In practise, the second metal would have been applied as a very thin layer 10 on the outside of the tube. As an alternative, the second metal could be applied on the inside of the tube. With this configuration, laser cutting or other conventional manufacturing methods, such as etching, can be applied as for a stent made from a single metal tube. Furthermore, such a stent would exhibit essentially the same mechanical properties as a stent made of the first metal only. The latter is, of course, only valid before and immediately after implantation in a vessel, i.e. before the start of any electrochemical process.

In this context, it should be noted that the normal corrosion process also is an electrochemical process, and if two or more metals are used in a stent, one (or all) of the metals will corrode and dissolve due to the normal corrosion mechanism, in addition to the corrosion driven by the galvanic element as described above. It should also be noted that it is possible to obtain "internal" galvanic elements if granules or small cells of a second metal are present in a first metal. The second metal may be present naturally in the first metal or may be implanted into the first metal by means of some suitable technique such as sintering. Obviously, the same effect would arise if the metal of which the stent is made comprises more than two metals with different electrochemical potentials. Such internal galvanic elements would accelerate the normal corrosion process and would also provide a further possibility to control the disintegration of the stent. With appropriate choice of metals, the same effect may also be utilized if an alloy or a compound of two or more metals is used for the manufacturing of the stents. Further, the stents have been described as comprising an expandable metal mesh; the inventive concept is, however, applicable on other stent configurations such as folded metal stents, or stents that have been rolled into a cylindrical configuration. Finally, it should be noted that herein the term "expandable" encompasses both self-expanding and non-self-expanding metal mesh stents.

Although the present invention has been described with reference to specific embodiments, also shown in the appended drawings, it will be apparent for those skilled in the art that many variations and modifications can be done within the scope of the invention as described in the specification and defined in the following claims.

Claims

1. Metal stent (1; 3; 7) for insertion into a body passage, **characterized in** that the metal stent (1; 3; 7) comprises a first metal that dissolves inside said body passage.

2. Metal stent (1; 3; 7) according to claim 1, **characterized in** that said first metal dissolves by corrosion inside said body passage.

3. Metal stent (1; 3; 7) according to claim 1, **characterized in** that said first metal dissolves by corrosion after a pre-defined time inside said body passage.

4. Metal stent (1) according to claim 2 or 3, further **characterized in** that the metal stent (1) is in the form of an expandable metal mesh (2), wherein at least parts of the expandable metal mesh (2) are made of said first metal.

5. Metal stent (1) according to claim 4, **characterized in** that the expandable metal mesh (2) is made of said first metal.

6. Metal stent (1) according to claim 4, **characterized in** that said parts of the expandable metal mesh (2) constitute joining parts of the expandable metal mesh (2).

7. Metal stent (3; 7) according to claim 1, further **characterized in** that metal stent (3; 7) also comprises a second metal, which has an electrochemical potential that differs from the electrochemical potential of the first metal, thereby forming a galvanic element that drives an electrochemical process in which the first metal is consumed inside said body passage.

8. Metal stent (3; 7) according to claim 7, **characterized in** that the first metal is consumed in said electrochemical process after a pre-defined time inside said body passage.

9. Metal stent (3; 7) according to claim 7 or claim 8, **characterized in** that the second metal dissolves by corrosion inside said body passage.

10. Metal stent (3; 7) according to claim 7 or claim 8, **characterized in** that the second metal dissolves by corrosion after a pre-defined time inside said body passage.

11. Metal stent (7) according to anyone of claims 7 to 10, **characterized in** that the second metal is provided as a thin layer on the first metal.

12. Metal stent (7) according to anyone of claims 7 to 10, **characterized in** that the second metal is provided as a thin layer on selected parts of the first metal.

13. Metal stent according to anyone of claims 7 to 10, **characterized in** that the second metal is provided as granules or cells within the first metal.

14. Metal stent according to anyone of claims 7 to 10, **characterized in** that the first metal and the second metal are in the form of an alloy or a compound.

15. Metal stent according to anyone of claim 7 to 14, **characterized in** that essentially all initial mechanical properties of the metal stent are given by the first metal.

16. Metal stent (3; 7) according to anyone of claims 7 to 10, further **characterized in** that the metal stent (3; 7) is in the form of an expandable metal mesh (4; 8), wherein joining parts of the expandable metal mesh (4; 8) are made of the first metal.

17. Metal stent (3; 7) according to anyone of claims 7 to 10, further **characterized in** that the metal stent (3; 7) is in the form of an expandable metal mesh (4; 8) and that the second metal is provided as a thin layer on selected part of the expandable metal mesh (4; 8).

18. Metal stent according to anyone of claims 7 to 17, further **characterized in** that the metal stent comprises more than two metals, all of which have different electrochemical potentials, thereby forming galvanic elements that each drives a respective electrochemical process in which the metal having the lower electrochemical potential is consumed.

19. Method for the manufacturing of a metal stent (7) that comprises a first metal and a second metal, the second metal having an electrochemical potential that differs from the electrochemical potential of the first metal, **characterized in** that the metal stent (7) is made from a tube of the first metal, the outer surface and/or the inner surface of the tube being coated with a layer of the second metal.

20. Method according to claim 19, further **characterized in** that the tube, which is made of the first metal, is coated with layers of several metals, all of which have different electrochemical potentials.

21. Method according to claim 18 or claim 20, **characterized in** that said manufacturing involves laser cutting or etching.

Abstract

The present invention provides a metal stent (1; 3; 7), which dissolves or disintegrates inside a body vessel after a predefined time. In a first embodiment, the metal stent (1) comprises an expandable metal mesh (2), which is made of a metal that dissolves by corrosion in the environment prevailing within the vessel. In another embodiment, the metal mesh (4; 8) is made of at least two metals having different electrochemical potentials, thereby forming an active galvanic element. In the galvanic element, an electrochemical reaction occurs, which consumes the metal having the lower electrochemical potential, thereby leaving the mesh (4; 8) in a disintegrated configuration.

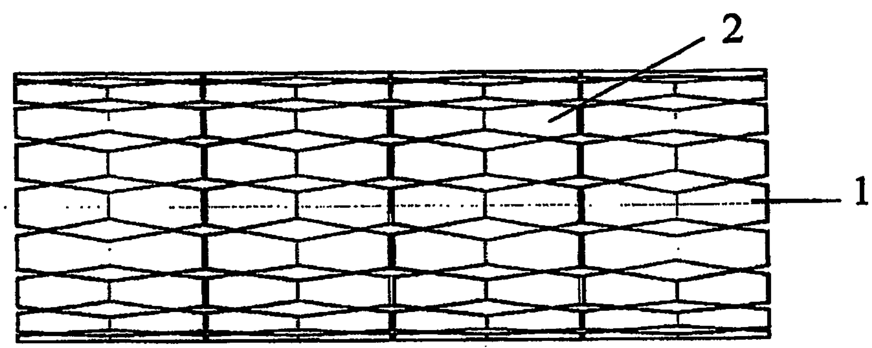

Fig. 1

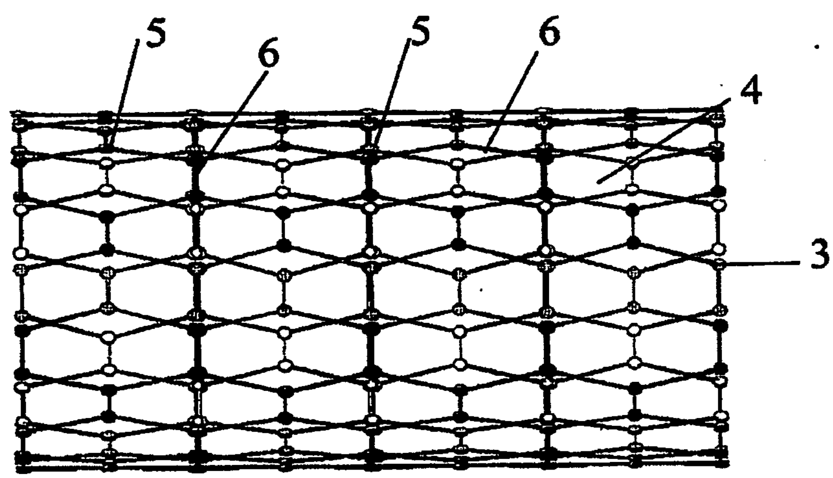

Fig. 2

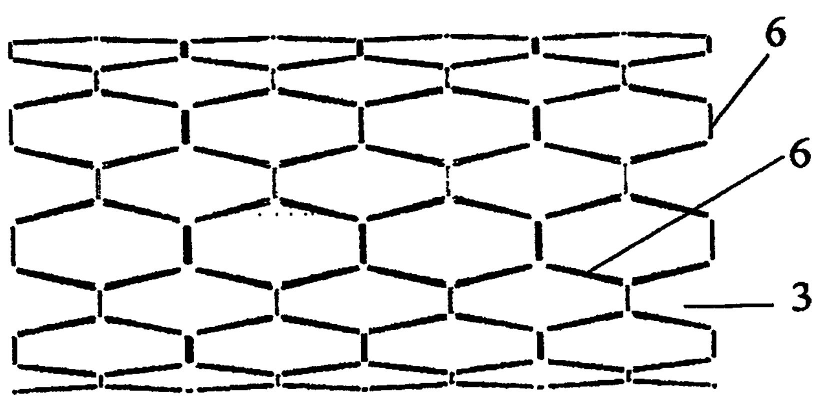

Fig. 3

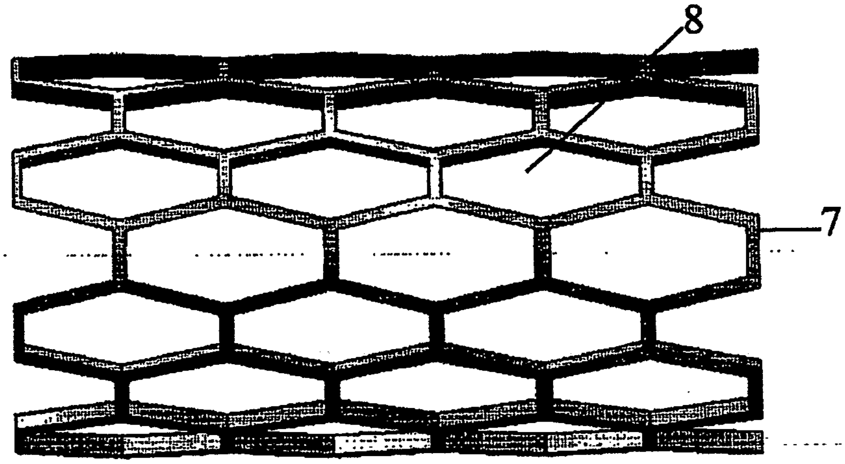

Fig. 4

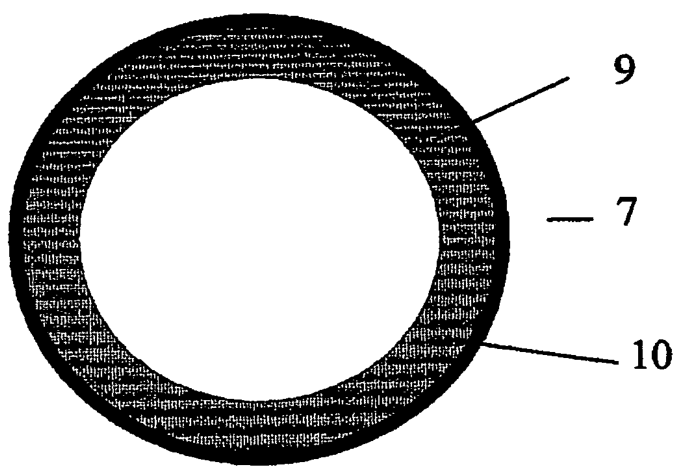

Fig. 5

This Page is Inserted by IFW Indexing and Scanning Operations and is not part of the Official Record

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images include but are not limited to the items checked:

- ☐ BLACK BORDERS
- ☐ IMAGE CUT OFF AT TOP, BOTTOM OR SIDES
- ☐ FADED TEXT OR DRAWING
- ☐ BLURRED OR ILLEGIBLE TEXT OR DRAWING
- ☐ SKEWED/SLANTED IMAGES
- ☒ COLOR OR BLACK AND WHITE PHOTOGRAPHS
- ☐ GRAY SCALE DOCUMENTS
- ☐ LINES OR MARKS ON ORIGINAL DOCUMENT
- ☐ REFERENCE(S) OR EXHIBIT(S) SUBMITTED ARE POOR QUALITY
- ☐ OTHER: ______________________

IMAGES ARE BEST AVAILABLE COPY.
As rescanning these documents will not correct the image problems checked, please do not report these problems to the IFW Image Problem Mailbox.